

# Isentress (raltegravir twice daily)

## Summary

Isentress (raltegravir twice daily) contains the anti-HIV drug raltegravir. Isentress belongs to the class of drugs called integrase inhibitors. Isentress is taken twice daily with or without food. Overall, Isentress was well-tolerated in clinical trials. General side effects were uncommon and included headache and diarrhea; these were usually mild and temporary.

## What is Isentress?

Isentress contains the anti-HIV drug raltegravir. Isentress belongs to the class of drugs called integrase inhibitors.

## How does Isentress work?

Isentress works by interfering with an enzyme needed by HIV called integrase. Using Isentress greatly reduces HIV's ability to infect cells and make copies of itself.

## How do people with HIV use Isentress?

Isentress is meant to be used as part of combination therapy for the treatment of HIV. Combinations of anti-HIV drugs are called ART (antiretroviral therapy).

For more information about HIV treatment, see CATIE's *Your Guide to HIV Treatment*.

For many people with HIV, the use of ART has increased their CD4+ cell counts and decreased the amount of HIV in their blood (viral load). These beneficial effects help to greatly reduce the risk of developing a life-threatening infection or an AIDS-related cancer. Neither Isentress nor any other treatment regimen (ART) is a cure for HIV. It is therefore important that you see your doctor for checkups and lab tests on a regular basis.

Evidence shows that HIV-positive people who are on ART, engaged in care, and have an ongoing undetectable viral load are substantially less likely

# FACT SHEET

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to transmit HIV to others, be it through sex, when sharing equipment to use drugs or during pregnancy and birth. In fact, the evidence for sexual transmission shows that people on ART who maintain an undetectable viral load do not pass HIV to their sexual partners. For further information see the CATIE fact sheet *HIV treatment and an undetectable viral load to prevent HIV transmission*. However, it is still a good idea to use condoms because they can reduce your risk for getting and passing on other sexually transmitted infections.

## Warnings

Although Isentress is generally well-tolerated, side effects can occur.

### 1. Skin—rash and hypersensitivity

In clinical trials, the most common side effect affecting the skin was rash; this is usually mild or moderate in severity and temporary.

Symptoms of hypersensitivity reactions can include severe rash or rash with a fever, together with lack of energy and painful muscles or joints. In severe cases additional symptoms can include peeling of the skin, blisters on the lips, swollen eyes and face, stomach cramps, and difficulty breathing. The manufacturer advises that Isentress (or any other drugs suspected of causing this reaction) should be discontinued immediately if these symptoms occur, otherwise the hypersensitivity reaction can become life threatening. If symptoms suggestive of hypersensitivity occur, see your doctor immediately or go to the emergency room of your nearest hospital or medical centre.

### 2. Muscles—soreness and/or weakness

Isolated cases of muscle-related weakness and aches have been reported in association with the use of Isentress. In some cases, affected people also had increased levels of the enzyme creatine kinase in the blood.

## Special populations

### Pregnant women

Isentress was the first integrase inhibitor approved in Canada in 2007. Data from more than 500 HIV-positive pregnant women who took Isentress twice daily as part of ART found that there was no overall increase in birth defects compared to births in HIV-negative women. This finding is encouraging. However, if you are pregnant or want to have a baby, talk to your doctor.

### Older people

Clinical trials of Isentress have not included large numbers of people who are 65 years or older so its effectiveness and safety in this population is not known.

## General side effects

In clinical trials, Isentress was well tolerated, generally safe and effective. However, as with any treatment, there were side effects but these were usually of mild to moderate intensity and temporary, such as the following:

- nausea
- diarrhea
- headache
- dizziness

Note that the HIV-positive people who are typically enrolled in pivotal clinical trials of HIV treatments, including Isentress, are generally young and healthy. Once a drug is approved and more widely available, it gets used by populations who are not usually in pivotal clinical trials. These people may be older and may have other health issues—such as cardiovascular disease, liver injury, kidney injury, type 2 diabetes, anxiety, depression, and substance use—that require medications or that cause symptoms. As a result, their experience of side effects may be different from those reported in pivotal clinical trials.

## Uncommon side effects

These side effects occurred in less than 2% of adults in clinical trials:

### Anxiety and depression

Although not common in clinical trials, a small proportion of people (less than 2%) who took Isentress-based combination therapy developed one or more of the following: depression, negative thoughts, anxiety and thoughts of suicide that in some cases led to attempted suicide.

Anxiety and depression are relatively common in HIV-positive people (regardless of whether they are on treatment or the type of treatment that they take). If you are taking Isentress and think that you may have developed anxiety or depression, speak to your doctor right away. Your doctor can help determine if you have anxiety or depression and if there is any relationship between them and the medicines that you are taking.

There have been reports of rare cases where people developed anxiety and/or depression after initiating treatment with Isentress-based regimens. Symptoms of anxiety and depression can include the following:

- becoming easily upset or angry
- feeling fearful
- excessive worry
- difficulty falling asleep or staying asleep, or waking up prematurely
- unexpected feelings of sadness
- recurrent nightmares
- prolonged feelings of sadness, anger or depression
- feeling hopeless
- loss of pleasure in everyday activities
- unexpectedly feeling tired or experiencing a lack of energy
- strange thoughts

If you experience any of the above, contact your doctor or nurse right away.

If you have thoughts of harming yourself or others, dial 911 right away.

## Drug interactions

Some drugs (including prescribed and over-the-counter), herbs and supplements can interfere with the absorption and/or effectiveness of Isentress. Such interference is called a drug interaction. Some drugs can reduce the levels of Isentress in your blood. This can make Isentress less effective and lead to treatment failure, possibly reducing your future treatment options. Other drugs can raise the levels of Isentress in your blood, resulting in enhanced side effects or new side effects. Therefore it is important to disclose to your doctor and pharmacist all the supplements, drugs, and herbs you are taking.

In general, Isentress does not have many drug interactions.

This factsheet is not comprehensive and only lists some of the potential and actual drug interactions with Isentress. Speak to your pharmacist to find out more about drug interactions with Isentress.

### Acid-reducing agents, laxatives, metal supplements and buffered medicines

Examples of acid-reducing agents (antacids) include the following:

- Alka-Seltzer
- Gaviscon (tablets and syrup)
- Maalox (liquid and tablets)
- Milk of Magnesia
- Pepto-Bismol
- Roloids
- Tums

Some antacids contain calcium while others contain magnesium or aluminum; some contain combinations of these metals. Merck, the drug manufacturer, warns that antacids containing aluminum or magnesium should *not* be taken with Isentress while antacids that contain calcium can be taken with Isentress. If you need to take antacids,

Speak to your pharmacist about ones that are safe for you to use. Remind your pharmacist that you are taking Isentress.

## Resistance and cross-resistance

Over time, as new copies of HIV are made in the body, the virus changes its structure. These changes, called mutations, can cause HIV to resist the effects of anti-HIV drugs, which means those drugs will no longer work for you.

To reduce the risk of developing drug resistance, all anti-HIV drugs should be taken every day exactly as prescribed and directed. If doses are delayed, missed or not taken as prescribed, the level of Isentress in the blood may fall too low. If this happens, the HIV in your body can become resistant to Isentress and possibly other drugs you are taking. If you find you are having problems taking your medications as directed, speak to your doctor, nurse or pharmacist about this. They can find ways to help you.

When HIV becomes resistant to one drug in a class, it sometimes becomes resistant to other drugs in that class. This is called cross-resistance. Feel free to talk with your doctor about your current and future treatment options. To help you decide what these future options might be, at some point your doctor can have a small sample of your blood analyzed to test for resistance.

## Dosage

Isentress is supplied as pink tablets. Each tablet contains 400mg raltegravir. The dose recommended by Merck for adults is 400 mg taken twice daily, together with other anti-HIV drugs. Isentress can be taken with or without food.

If you forget to take a dose, Merck recommends that “you take it as soon as you remember. If you do not remember until it is time for your next dose, skip the missed dose and go back to your regular schedule.”

## Availability

Isentress is licensed in Canada. Your doctor or pharmacist can tell you more about the availability and coverage of Isentress in your region. CATIE’s online module *Federal, Provincial and Territorial Drug Access Programs* also contains information about Canadian drug coverage.

## References

Merck Canada. Isentress (raltegravir tablets). *Product Monograph*. 19 September, 2018.

Lee FJ, Amin J, Bloch M, et al. Skeletal muscle toxicity associated with raltegravir-based combination antiretroviral therapy in HIV-infected adults. *Journal of Acquired Immune Deficiency Syndromes*. 2013 Apr 15;62(5):525-33.

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## Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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